

Europäisches Patentamt
European Patent Office
Office européen des brevets



(11) **EP 0 898 972 A2**

(12) **EUROPEAN PATENT APPLICATION**

(43) Date of publication:
03.03.1999 Bulletin 1999/09

(51) Int. Cl.⁶: **A61L 27/00**

(21) Application number: 98115184.8

(22) Date of filing: 12.08.1998

(84) Designated Contracting States:
AT BE CH CY DE DK ES FI FR GB GR IE IT LI LU
MC NL PT SE
Designated Extension States:
AL LT LV MK RO SI

(30) Priority: 20.08.1997 JP 224049/97

(71) Applicant: Menicon Co., Ltd.
Nagoya-shi Aichi-ken (JP)

(72) Inventors:
• Ojio, Tatsuya
Kasugai-shi, Aichi (JP)

• Niwa, Kazuharu
Kasugai-shi, Aichi (JP)
• Kawaguchi, Tohru
Kasugai-shi, Aichi (JP)

(74) Representative:
Hartz, Nikolai F., Dr. et al
Wächtershäuser & Hartz,
Patentanwälte,
Tal 29
80331 München (DE)

(54) **Soft intraocular lens material**

(57) A soft intraocular lens material which consists essentially of a polymer obtained by polymerizing polymerizable components containing a hydrophilic monomer, and which has a water absorptivity of from 1.5 to 4.5 wt%.

EP 0 898 972 A2

Description

[0001] The present invention relates to a soft intraocular lens material. More specifically, it relates to a soft intraocular lens material which is excellent in flexibility and has a high refractive index, whereby the lens can be made thin and can be folded so that it can be inserted through a small incision, and which is yet excellent in transparency and free from so-called glistenings i.e. a phenomenon whereby such transparency is lost.

[0002] In order to minimize the injury to the eye by cataract operation using an intraocular lens, it is usually advisable to minimize the incision for the surgical operation. As phacoemulsification has progressed wherein a crystalline lens is fractured by ultrasonic vibration, and its fragments are suctioned by means of a small cannula, it has been made possible to remove a crystalline lens through an incision not larger than 2 or 3 mm.

[0003] However, an intraocular lens usually has a diameter of about 6 mm, and to insert such an intraocular lens as it is, it is necessary to incise the portion for insertion to a large extent. Accordingly, in recent years, various intraocular lenses of soft type which are soft, flexible and swellable, have been invented, whereby insertion through a small incision has been made possible.

[0004] As such intraocular lenses, there have been proposed, for example, an intraocular lens obtained by copolymerizing a monomer mixture comprising at least two types of (meth)acrylate monomers having aromatic rings, and a crosslinkable monomer (JP-A-4-292609), a soft intraocular lens obtained by using components comprising a perfluorooctylethyloxypropylene (meth)acrylate monomer, a 2-phenylethyl (meth)acrylate monomer, an alkyl (meth)acrylate and a crosslinkable monomer (JP-A-8-224295), and an intraocular lens obtained by using a monomer, of which the refractive index of the homopolymer is at least 1.5, a monomer, of which the glass transition temperature of the homopolymer is lower than 30°C, and a crosslinkable monomer (JP-A-8-503506).

[0005] Each of these intraocular lenses has transparency and flexibility and is deformable, and each of them can accordingly be inserted through a relatively small incision. However, they have a drawback that when they are implanted in the eyes, white dots appear in the lenses by hydration, whereby so-called glistenings take place i.e. a phenomenon whereby the transparency is substantially lowered or lost.

[0006] In addition to those mentioned above, for example, an intraocular lens material employing a hydroxyalkyl (meth)acrylate and a ring structure- or halogen atom-containing (meth)acrylate and/or (meth)acrylamide derivative as the main components (JP-A-6-22565), an ocular lens material for e.g. an intraocular lens, obtained by using a composition comprising a (meth)acrylate having a hydroxyl group and a phenoxy group which may be substituted, and a crosslinking agent (JP-A-8-173522), and a soft intraocular lens material employing an aromatic ring-containing acrylate and a fluorine atom-containing alkyl acrylate as the main components (JP-A-9-73052), have been proposed.

[0007] Each of these materials is excellent in flexibility and has a large shape-regaining force and thus can be inserted through a small incision. However, when they are implanted in the eyes, their transparency likewise tends to decrease by a temperature change. Therefore, it has been desired to develop an intraocular lens which is free from such a decrease in the transparency (glistenings).

[0008] The present invention has been made in view of the above-mentioned prior art, and it is an object of the present invention to provide a soft intraocular lens material which is excellent in flexibility and has a high refractive index, whereby the lens can be made thin and can be folded and inserted through a small incision, and which is capable of presenting a soft intraocular lens which is excellent in transparency and free from glistenings.

[0009] The present invention provides a soft intraocular lens material which consists essentially of a polymer obtained by polymerizing polymerizable components containing a hydrophilic monomer, and which has a water absorptivity of from 1.5 to 4.5 wt%.

[0010] Now, the present invention will be described in detail with reference to the preferred embodiments.

[0011] As mentioned above, the soft intraocular lens material of the present invention consists essentially of a polymer obtained by polymerizing polymerizable components containing a hydrophilic monomer, and has a water absorptivity of from 1.5 to 4.5 wt%.

[0012] The most important object of the present invention is to provide a material which is capable of providing a soft intraocular lens having excellent properties such that it shows excellent transparency and is free from glistenings. Heretofore, various researches relating to maintenance of excellent transparency have been made, since the transparency of e.g. an acrylic soft intraocular lens tends to gradually decrease and in some cases, be lost to such an extent as to cause a problem in the viewing function, when such an intraocular lens is implanted in the eye. Here, the present inventors have conducted an extensive study by paying a particular attention to the temperature change before and after the implantation of the intraocular lens, the relation between the water content in the material of the intraocular lens and the glistenings, and the relation between agglomeration of water in the material due to the temperature change and the glistenings. As a result, it has been found possible to obtain a material whereby excellent transparency can be maintained without glistenings in spite of a temperature change, on the basis of a concept such that by incorporating or uniformly dispersing units based on a hydrophilic monomer, as constituting units in a material having a low water absorptivity which is usually susceptible to glistenings, the contained water is also dispersed, and agglomeration of water (glisten-

ings) will not take place.

[0013] The polymer to be used in the present invention is one obtained by polymerizing polymerizable components containing a hydrophilic monomer (hereinafter referred to as the hydrophilic monomer (B)).

[0014] The hydrophilic monomer (B) becomes essential constituting units in the resulting soft intraocular lens material, as mentioned above, and is a component having a function to promote the lowering of glistenings in the soft intraocular lens material.

[0015] Typical examples of the hydrophilic monomer (B) include a hydroxyl group-containing alkyl (meth)acrylate wherein the alkyl group has from 1 to 20 carbon atoms (hereinafter referred to as a monomer (B-1)), a (meth)acrylamide monomer (hereinafter referred to as a monomer (B-2)), an N-vinyl lactam (hereinafter referred to as a monomer (B-3)), and a hydrophilic monomer (hereinafter referred to as a monomer (B-4)) other than such monomers (B-1), (B-2) and (B-3). At least one member selected from these monomers can be suitably used.

[0016] The monomer (B-1) may, for example, be a hydroxyalkyl (meth)acrylate such as hydroxyethyl (meth)acrylate, hydroxypropyl (meth)acrylate, hydroxybutyl (meth)acrylate or hydroxypentyl (meth)acrylate, or a dihydroxyalkyl (meth)acrylate such as dihydroxypropyl (meth)acrylate, dihydroxybutyl (meth)acrylate or dihydroxypentyl (meth)acrylate. These monomers can be used alone or in combination as a mixture of two or more of them.

[0017] The monomer (B-2) may, for example, be an N,N-dialkyl (meth)acrylamide such as N,N-dimethyl (meth)acrylamide, N,N-diethyl (meth)acrylamide or N,N-dipropyl (meth)acrylamide; or an N,N-dialkylaminoalkyl (meth)acrylamide such as N,N-dimethylaminopropyl (meth)acrylamide or N,N-diethylaminopropyl (meth)acrylamide. These monomers may be used alone or in combination as a mixture of two or more of them.

[0018] The monomer (B-3) may, for example, be N-vinylpyrrolidone, N-vinylpiperidone or N-vinylcaprolactam. These monomers may be used alone or in combination as a mixture of two or more of them.

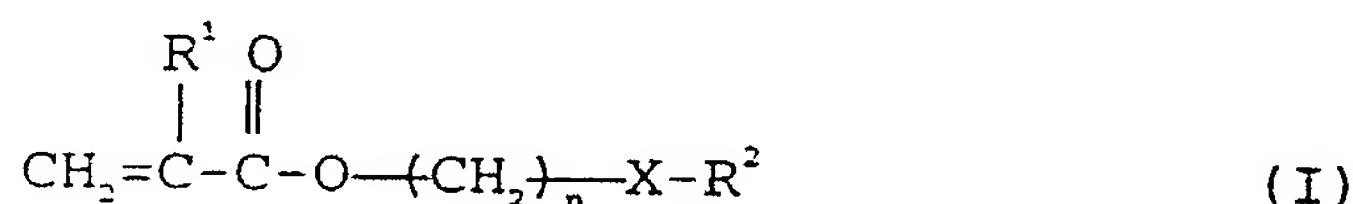
[0019] The monomer (B-4) may, for example, be diethylene glycol mono(meth)acrylate, triethylene glycol mono(meth)acrylate, propylene glycol mono(meth)acrylate, (meth)acrylic acid, methoxyethyl (meth)acrylate, ethoxyethyl (meth)acrylate, maleic anhydride, maleic acid, a maleic acid derivative, fumaric acid, a fumaric acid derivative, an aminostyrene or a hydroxystyrene. These monomers may be used alone or in combination as a mixture of two or more of them.

[0020] Among the above hydrophilic monomers (B), the above monomers (B-1) and (B-2) are preferred, and 2-hydroxyethyl methacrylate is particularly preferred, since the function to promote the lowering of glistening is large.

[0021] In order to sufficiently obtain the effect to promote the lowering of glistenings, the content of the hydrophilic monomer (B) in the polymerizable components, is usually at least 7 wt%, preferably at least 10 wt%. Further, in order to eliminate the possibility of a decrease in the flexibility or a decrease in the refractive index or the shape-restoration property of the soft intraocular lens material, it is usually at most 45 wt%, preferably at most 42 wt%.

[0022] The polymerizable components to obtain the polymer to be used in the present invention, may contain, in addition to the above hydrophilic monomer (B) other polymerizable monomers copolymerizable with such a hydrophilic monomer (B), as the case requires.

[0023] Typical examples of such other polymerizable monomers include an aromatic ring-containing (meth)acrylate (hereinafter referred to as a (meth)acrylate (A)) of the formula (I):



wherein R^1 is a hydrogen atom or a methyl group, R^2 is an aromatic ring which may be substituted by at least one substituent, such as a C_{1-10} alkyl group or a halogen atom such as a fluorine atom, a chlorine atom or a bromine atom, X is an oxygen atom or a direct bond, and n is an integer of from 0 to 5, an alkyl (meth)acrylate wherein the alkyl group has from 1 to 20 carbon atoms (hereinafter referred to as an alkyl (meth)acrylate (C)) other than the above-mentioned monomer (B-1), and a crosslinkable monomer (hereinafter referred to as a crosslinkable monomer (D)).

[0024] The above (meth)acrylate (A) is a component having a function to improve the refractive index of the resulting soft intraocular lens material.

[0025] Specific examples of the (meth)acrylate (A) include phenoxyethyl (meth)acrylate, phenylethyl (meth)acrylate, benzyl (meth)acrylate, phenyl (meth)acrylate and pentabromophenyl (meth)acrylate. These acrylates may be used alone or in combination as a mixture of two or more of them. Among them, it is preferred to use at least one member selected from phenoxyethyl acrylate, phenylethyl acrylate and benzyl acrylate, as the effect to improve the refractive index of the resulting soft intraocular lens material is large. Particularly preferred is phenoxyethyl acrylate, since in addition to the above refractive index, the flexibility can also be improved.

[0026] The above alkyl (meth)acrylate (C) is a component having a function to improve the flexibility and the shape

restoration property of the soft intraocular lens material.

[0027] Specific examples of the alkyl (meth)acrylate (C) include a linear, branched or cyclic alkyl (meth)acrylate such as methyl acrylate, ethyl acrylate, propyl acrylate, butyl acrylate, pentyl acrylate, hexyl acrylate, heptyl acrylate, nonyl acrylate, stearyl (meth)acrylate, octyl (meth)acrylate, decyl (meth)acrylate, lauryl (meth)acrylate, pentadecyl (meth)acrylate, 2-ethylhexyl (meth)acrylate, cyclopentyl acrylate or cyclohexyl acrylate; and a fluorine-containing alkyl (meth)acrylate such as 2,2,2-trifluoroethyl (meth)acrylate, 2,2,3,3-tetrafluoropropyl (meth)acrylate, 2,2,3,3-tetrafluoro-t-pentyl (meth)acrylate, 2,2,3,4,4,4-hexafluorobutyl (meth)acrylate, 2,2,3,4,4,4-hexafluoro-t-hexyl (meth)acrylate, 2,3,4,5,5,5-hexafluoro-2,4-bis(trifluoromethyl)pentyl (meth)acrylate, 2,2,3,3,4,4-hexafluorobutyl(meth)acrylate, 2,2,2,2',2',2'-hexafluoroisopropyl (meth)acrylate, 2,2,3,3,4,4,4-heptafluorobutyl (meth)acrylate or 2,2,3,3,4,4,5,5-octafluoropentyl (meth)acrylate. These compounds may be used alone or in combination as a mixture of two or more of them. Among these compounds, preferred is an alkyl acrylate wherein the alkyl group has from 1 to 5 carbon atoms, and particularly preferred is ethyl acrylate and/or butyl acrylate, since the effect to improve the flexibility and the shape restoration property of the resulting soft intraocular lens material is large.

[0028] The above crosslinkable monomer (D) is a component having a function to impart good mechanical strength, to further improve the shape restoration property or to improve the copolymerizability of the hydrophilic monomer (B) or the polymerizable components such as other polymerizable monomers to one another.

[0029] Specific examples of the crosslinkable monomer (D) include butanediol di(meth)acrylate, ethylene glycol di(meth)acrylate, diethylene glycol di(meth)acrylate, triethylene glycol di(meth)acrylate, propylene glycol di(meth)acrylate, dipropylene glycol di(meth)acrylate, diallyl fumarate, allyl (meth)acrylate, vinyl (meth)acrylate, trimethylolpropane tri(meth)acrylate, methacryloyloxyethyl (meth)acrylate, divinylbenzene, diallylphthalate, diallyl adipate, triallyl diisocyanate, α -methylene-N-vinylpyrrolidone, 4-vinylbenzyl (meth)acrylate, 3-vinylbenzyl (meth)acrylate, 2,2-bis((meth)acryloyloxyphenyl)hexafluoropropane, 2,2-bis((meth)acryloyloxyphenyl)propane, 1,4-bis(2-(meth)acryloyloxyhexafluoroisopropyl)benzene, 1,3-bis(2-(meth)acryloyloxyhexafluoroisopropyl)benzene, 1,2-bis(2-(meth)acryloyloxyhexafluoroisopropyl)benzene, 1,4-bis(2-(meth)acryloyloxyisopropyl)benzene, 1,3-bis(2-(meth)acryloyloxyisopropyl)benzene and 1,2-bis(2-(meth)acryloyloxyisopropyl)benzene. These monomers may be used alone or in combination as a mixture of two or more of them. Among them, butanediol di(meth)acrylate and ethylene glycol di(meth)acrylate are particularly preferred from the viewpoint such that the effect to impart good mechanical strength and to improve the copolymerizability and the shape restoration property, is large.

[0030] It is preferred to suitably adjust the content of such other polymerizable monomers in the polymerizable components, so that the effect by the above hydrophilic monomer (B) is sufficiently obtained, so that the effects of the respective polymerizable monomers can adequately be obtained and so that the copolymerizability of the polymerizable components to one another is maintained, and it is adjusted so that the total amount of the polymerizable components inclusive of the hydrophilic monomer (B), will be 100 wt%. Namely, the content of other polymerizable monomers in the polymerizable components is usually at least 55 wt%, preferably at least 58 wt%, and usually at most 93 wt%, preferably at most 90 wt%.

[0031] In the present invention, it is particularly preferred to employ a polymer obtained by polymerizing polymerizable components comprising the above (meth)acrylate (A), at least one hydrophilic monomer (B) selected from the monomers (B-1), (B-2) and (B-3), the alkyl (meth)acrylate (C) and the crosslinkable monomer (D), since the effects to improve the flexibility of the resulting soft intraocular lens material, to impart a high refractive index and to maintain the excellent transparency irrespective of the temperature change, without glistenings, can be obtained more remarkably.

[0032] When the (meth)acrylate (A), the hydrophilic monomer (B), the alkyl (meth)acrylate (C) and the crosslinkable monomer (D) are used in combination as mentioned above, the amounts of the respective components are preferably adjusted as follows.

[0033] In order to adequately increase the refractive index of the resulting soft intraocular lens material, the weight ratio of the (meth)acrylate (A) to the alkyl (meth)acrylate (C) (i.e. the (meth)acrylate (A)/the alkyl (meth)acrylate (C)), is preferably adjusted to be at least 10/90, preferably at least 15/85. Further, in order to adequately obtain the effect to improve the shape restoration property of the soft intraocular lens material and the effect to control the flexibility, the weight ratio is preferably adjusted to be at most 95/5, preferably at most 80/20.

[0034] Further, the amount of the above hydrophilic monomer (B) is preferably adjusted to be at least 10 parts by weight, preferably at least 13 parts by weight, per 100 parts by weight of the total amount of the (meth)acrylate (A) and the alkyl (meth)acrylate (C), in order to adequately obtain the effect to promote the lowering of glistenings, and it is preferably adjusted to be at most 45 parts by weight, preferably at most 42 parts by weight, per 100 parts by weight of the above total amount, in order to eliminate the possibility of a decrease in the refractive index and the shape restoration property of the soft intraocular lens material or a decrease in the flexibility.

[0035] Further, the amount of the above crosslinkable monomer (D) is preferably adjusted to be at least 0.1 part by weight, preferably at least 0.5 part by weight, per 100 parts by weight of the total amount of the (meth)acrylate (A) and the alkyl (meth)acrylate (C) in order to control the flexibility of the resulting soft intraocular lens material and to adequately obtain the effect to improve the copolymerizability and the shape restoration property. Further, it is preferably

adjusted to be at most 10 parts by weight, preferably at most 5 parts by weight, per 100 parts by weight of the above total amount, in order to eliminate the possibility of a decrease in the flexibility of the soft intraocular lens material or a decrease in the shape restoration property.

[0036] Further, in the present invention, from the viewpoint of safety, an ultraviolet absorber or a dyestuff which scarcely elutes from the soft intraocular lens material, may be added to the polymerizable components, as the case requires.

[0037] Typical examples of the ultraviolet absorber include benzophenones such as 2-hydroxy-4-methoxybenzophenone and 2-hydroxy-4-octoxybenzophenone, benzotriazoles such as 2-(2'-hydroxy-5'-methacryloxyethyleneoxy-t-butylphenyl)-5-methyl-benzotriazole, 2-(2'-hydroxy-5'-methylphenyl)benzotriazole and 5-chloro-2(3'-t-butyl-2'-hydroxy-5'-methylphenyl)benzotriazole, salicylic acid derivatives, and hydroxyacetophenone derivatives. Further, a reactive ultraviolet absorber may also be employed which has the same chemical structure portion as the above-mentioned ultraviolet absorbers and which has a portion polymerizable with the polymerizable components in the present invention. These ultraviolet absorbers may be used alone or in combination as a mixture of two or more of them.

[0038] The amount of the ultraviolet absorber is preferably adjusted to be at least 0.01 part by weight, preferably at least 0.05 part by weight, per 100 parts by weight of the total amount of the polymerizable components, and it is preferably adjusted to be at most 5 parts by weight, preferably at most 3 parts by weight, per 100 parts by weight of the total amount of the polymerizable components.

[0039] The above dyestuff is preferably a yellow or orange dyestuff, in order to correct, by the soft intraocular lens, blue vision of a patient having no crystalline lens after the cataract operation. Typical examples of such a dyestuff include an oil-soluble dyestuff such as CI Solvent Yellow or CI Solvent Orange as disclosed in Color Index (CI), a disperse dye such as CI Disperse Yellow or CI Disperse Orange, and a vat dye. Further, it is also possible to use a reactive dye which has same chemical structural portion as these dyes and which has a portion polymerizable with the polymerizable components of the present invention. These dyestuffs may be used alone or in combination as a mixture of two or more of them.

[0040] The amount of the above dyestuff is preferably adjusted to be at least 0.001 part by weight, preferably at least 0.01 part by weight, per 100 parts by weight of the total amount of the polymerizable components, so that the resulting soft intraocular lens material is sufficiently colored. Further, it is preferably adjusted to be at most 5 parts by weight, preferably at most 3 parts by weight, per 100 parts by weight of the total amount of the polymerizable components, so that the material will not be excessively deeply colored.

[0041] The soft intraocular lens material of the present invention can be obtained by blending, if necessary, a ultraviolet absorber or a dyestuff to the polymerizable components comprising the hydrophilic monomer (B) and, if necessary, other polymerizable monomers, and then adding e.g. a radical polymerization initiator thereto, followed by polymerization by a usual method.

[0042] The usual method may, for example, be a method which comprises incorporating a radical polymerization initiator which is commonly used for polymerization, to the polymerizable components and then gradually heating the mixture within a temperature range of from room temperature to about 130°C, or a method which comprises irradiating electromagnetic waves such as microwaves, ultraviolet rays or radiation rays (γ -rays) to carry out the polymerization. In the case of the heat polymerization, the temperature may stepwisely be raised. Further, the polymerization may be conducted by a bulk polymerization method or a solvent polymerization method by means of a solvent, or it may be conducted by any other methods.

[0043] Typical examples of the above radical polymerization initiator include azobisisobutyronitrile, azobisdimethylvaleronitrile, benzoyl peroxide, t-butyl hydroperoxide, and cumene hydroperoxide. These initiators may be used alone or in combination as a mixture of two or more of them.

[0044] In a case where polymerization is carried out by means of light rays, a photopolymerization initiator or a sensitizer may preferably be incorporated.

[0045] Typical examples of the above photopolymerization initiator include benzoin type photopolymerization initiators such as methylorthobenzoyl benzoate, methylbenzoyl formate, benzoin methyl ether, benzoin ethyl ether, benzoin isopropyl ether, benzoin isobutyl ether and benzoin n-butyl ether; phenone type photopolymerization initiators such as 2-hydroxy-2-methyl-1-phenylpropan-1-one, p-isopropyl- α -hydroxyisobutylphenone, p-t-butyltrichloroacetophenone, 2,2-dimethoxy-2-phenylacetophenone, α,α -dichloro-4-phenoxyacetophenone and N,N-tetraethyl-4,4-diaminobenzophenone; 1-hydroxycyclohexylphenylketone; 1-phenyl-1,2-propanedione-2-(o-ethoxycarbonyl)oxime; thioxanthone type photopolymerization initiators such as 2-chlorothioxanthone and 2-methylthioxanthone; dibenzosuberone; 2-ethylanthraquinone; benzophenone acrylate; benzophenone; and benzyl.

[0046] The amount of the above polymerization initiator or the sensitizer is preferably adjusted to be at least 0.002 part by weight, preferably at least 0.01 part by weight, per 100 parts by weight of the total amount of the polymerizable components to let the polymerization reaction proceed at an adequate rate. Further, it is preferably adjusted to be at most 10 parts by weight, preferably at most 2 parts by weight, per 100 parts by weight of the polymerizable components to prevent formation of bubbles in the resulting soft intraocular lens material.

[0047] When the soft intraocular lens material of the present invention is shaped into soft intraocular lenses, shaping methods which are commonly employed by those skilled in the art, may be employed. As such shaping methods, a cutting and grinding method and a molding method may, for example, be mentioned. The cutting and grinding method is a method in which polymerization of the polymerizable components is carried out in a suitable mold or vessel designed to facilitate shaping of an intraocular lens, to obtain a rod-, block- or plate-shaped base material (polymer), and then the base material is processed into a desired shape by mechanical processing such as cutting, grinding and polishing. The molding method is a method wherein a mold corresponding to the shape of a desired intraocular lens is prepared, and the polymerization of the above polymerizable components is carried out in this mold to obtain a polymer (a molded product), which may further be subjected to mechanical finishing treatment, if necessary. The above-mentioned mold or vessel wherein polymerization of the polymerizable components is carried out, may be one made of glass or a plastic such as polyethylene or polypropylene.

[0048] Apart from these methods, in the present invention, it is also possible to employ a method wherein a monomer capable of imparting a hard nature is impregnated to a soft intraocular lens material, then the monomer is polymerized to harden the entire material, which is then subjected to cutting and grinding to obtain a shaped product processed to have a desired shape, whereupon the hard polymer is removed from the shaped product to obtain a shaped product (a soft intraocular lens) made of a soft intraocular lens material (JP-A-62-278041, JP-A-1-11854).

[0049] When a soft intraocular lens is prepared from the soft intraocular lens material of the present invention, a supporting portion of the lens may be prepared separately from the lens, and a hole may be formed in the lens so that the supporting portion may be attached to the lens by inserting it into the hole, or it may be molded simultaneously (integrally) with the lens.

[0050] The soft intraocular lens material of the present invention thus obtainable, has a water absorptivity of from 1.5 to 4.5 wt%. As mentioned above, it is a non-water absorptive material having such a specific water absorptivity and containing units based on a hydrophilic monomer (B) as constituting units, whereby the excellent transparency can be maintained without glistenings, which are likely to take place with conventional materials. If the water absorptivity of such a soft intraocular lens material is less than 1.5 wt%, glistenings tend to occur even by a slight temperature change. The water absorptivity is preferably at least 1.6 wt%, so that glistenings scarcely occur even if the temperature change is large. On the other hand, if the water absorptivity exceeds 4.5 wt%, the flexibility tends to decrease, and the shape restoration property tends to decrease, although no glistening problem will occur. The water absorptivity is preferably at most 4.4 wt%, so that the decrease in the flexibility or the decrease in the shape restoration property tends to be less likely to occur.

[0051] In the present invention, the water absorptivity is a value obtained by the following formula.

$$\text{Water absorptivity (wt\%)} = \{(W - W_0) / W_0\} \times 100$$

This is a value with respect to a test specimen having a thickness of 1.0 mm at 25°C. In the formula, W is the weight (g) of the test specimen upon absorption of water to the equilibrium state, and W_0 is the weight (g) of the test specimen in a dried state.

[0052] The soft intraocular lens material of the present invention is one having an excellent property such that no glistenings will occur even when a temperature change occurs, as mentioned above. Such a temperature change is a temperature change within a range of a usual environmental temperature at which the intraocular lens is used, i.e. a range including a common body temperature of from 36 to 37°C. For example, it may be a temperature change of about 15°C from about 40°C to about 25°C, or at least a temperature change of about 5°C from about 40°C to about 35°C.

[0053] As described in the foregoing, the soft intraocular lens material of the present invention is excellent in flexibility and has a high refractive index, whereby the lens can be made thin and can be folded and inserted through a small incision. Further, it is a soft intraocular lens material which is excellent in transparency and free from glistenings.

[0054] Now, the soft intraocular lens material of the present invention will be described in further detail with reference to Examples. However, it should be understood that the present invention is by no means restricted to such specific Examples.

EXAMPLE 1 to 21 and COMPARATIVE EXAMPLES 1 to 6

[0055] The polymerizable components as identified in Table 1 or 2 and 1 part by weight, per 100 parts by weight of the total amount of the polymerizable components, of 2,2'-azobis(2,4-dimethylvaleronitrile), as a polymerization initiator, were mixed, and the mixture was poured into a casting mold having a desired intraocular lens shape. This casting mold was put into an oven and heat polymerization molding was carried out at 50°C for 24 hours. Then, the casting mold was transferred to an air circulating dryer and heated to from 65 to 130°C at a rate of 10°C/hr and then cooled to room temperature. Then, light irradiation was carried out over one hour by means of an irradiation apparatus (black light, manufactured by Matsushita Electric Industrial Co., Ltd.). Thereafter, the obtained polymer was taken out from the

casting mold and further dried for 2 days at 50°C in an oven to obtain a soft intraocular lens material having a thickness of 1 mm.

[0056] Abbreviations used in Tables 1 and 2 are as follows.

(Meth)acrylate (A)

[0057]

POEA: 2-Phenoxyethyl acrylate
POEMA: 2-Phenoxyethyl methacrylate
PEA: Phenylethyl acrylate
PEMA: Phenylethyl methacrylate

Hydrophilic monomer (B)

[0058]

HEMA: 2-Hydroxyethyl methacrylate
HEA: 2-Hydroxyethyl acrylate
NVP: N-Vinylpyrrolidone
DMAA: N,N-Dimethylacrylamide
HBMA: 2-Hydroxybutyl methacrylate

Alkyl (meth)acrylate (C)

[0059]

EA: Ethyl acrylate
iBuA: Isobutyl acrylate
3FEA: 2,2,2-Trifluoroethyl acrylate

Crosslinkable monomer (D)

[0060]

BDDA: Butanediol diacrylate
EDMA: Ethylene glycol dimethacrylate
BDDMA: Butanediol dimethacrylate

[0061] The amounts of the hydrophilic monomer (B) and the crosslinkable monomer (D) in Tables 1 and 2 are amounts by parts by weight per 100 parts by weight of the total amount of the (meth)acrylate (A) and the alkyl (meth)acrylate (C). However, in Example 21, the sum of the hydrophilic monomer (B) and the alkyl (meth)acrylate (C) becomes 100 wt%.

Table 1

Example No.	Polymerizable components (parts by weight)							
	(Meth)acrylate (A)		Hydrophilic monomer (B)		Alkyl (meth)acrylate (C)		Crosslinkable monomer (D)	
1	POEA	(20)	HEMA	(15)	EA	(80)	EDMA	(4)
2	POEA	(20)	HEMA	(25)	EA	(80)	EDMA	(4)
3	POEA	(40)	HEMA	(15)	EA	(60)	BDDA	(4)
4	POEA	(40)	HEMA	(25)	EA	(60)	EDMA	(4)
5	POEA	(60)	HEMA	(15)	EA	(40)	BDDA	(4)

Table 1 (continued)

Example No.	Polymerizable components (parts by weight)							
	(Meth)acrylate (A)		Hydrophilic monomer (B)		Alkyl (meth)acrylate (C)		Crosslinkable monomer (D)	
6	POEA	(60)	HEMA	(15)	EA	(40)	EDMA	(4)
7	POEA	(60)	HEMA	(15)	EA	(40)	BDDMA	(4)
8	POEA	(60)	HEMA	(20)	EA	(40)	BDDA	(4)
9	POEA	(60)	HEMA	(25)	EA	(40)	BDDA	(4)
10	POEA	(60)	HEMA	(30)	3FEA	(40)	EDMA	(2)
11	POEA	(60)	HEMA	(40)	EA	(40)	BDDA	(4)
12	POEA	(60)	HEA	(15)	EA	(40)	BDDA	(4)
13	POEA	(60)	HEA	(25)	EA	(40)	BDDA	(4)

Table 2

Example No.	Polymerizable components (parts by weight)							
	(Meth)acrylate (A)		Hydrophilic monomer (B)		Alkyl (meth)acrylate (C)		Crosslinkable monomer (D)	
14	POEA	(60)	NVP	(15)	EA	(40)	BDDA	(4)
15	POEA	(60)	NVP	(25)	EA	(40)	BDDA	(4)
16	POEA	(60)	DMAA	(15)	EA	(40)	BDDA	(5)
17	POEA	(60)	DMAA	(25)	EA	(40)	BDDA	(4)
18	POEA	(60)	HBMA	(30)	EA	(40)	BDDA	(4)
19	POEA	(70)	HEMA	(15)	EA	(30)	BDDA	(4)
20	POEMA	(30)	HEMA	(15)	EA	(70)	BDDA	(2)
21	-	-	HEMA	(20)	iBuA	(80)	-	-
Comp. Ex.								
1	POEA	(60)	-	-	EA	(40)	BDDA	(4)
2	POEA	(60)	-	-	3FEA	(40)	EDMA	(2)
3	POEA	(60)	HEMA	(6)	3FEA	(40)	EDMA	(2)
4	PEA	(67)	-	-	-	-	BDDA	(3.5)
	PEMA	(33)	-	-	-	-	-	-
5	POEA	(60)	HEMA	(10)	EA	(40)	BDDA	(4)
6	POEA	(60)	HEMA	(60)	EA	(40)	BDDA	(4)

[0062] Then, as the physical properties of the obtained soft intraocular lens materials, the water absorptivity, the transparency (evaluation of glistenings), the flexibility and the shape restoration property were examined in accordance with the following methods. The results are shown in Table 3.

(a) Water absorptivity

[0063] A test specimen having a thickness of 1.0 mm was prepared from the soft intraocular lens material, and the water absorptivity of this test specimen at 25°C was obtained by the following formula.

$$\text{Water absorptivity (wt\%)} = \{(W - W_0) / W_0\} \times 100$$

wherein W is the weight (g) of the test specimen upon absorption of water to the equilibrium state, and W₀ is the weight (g) of the test specimen in a dried state.

(b) Transparency (evaluation of glistenings)

[0064] The soft intraocular lens material was immersed in water at 40°C for 3 hours and then in water at 25°C or 35°C for 1 hour, whereupon the appearance (transparency) of this soft intraocular lens material was visually observed under irradiation of a transmitted light by means of a projector (V-12B, manufactured by Nikon K.K.), and evaluated on the basis of the following evaluation standards.

Evaluation standards

[0065]

- A: Excellent transparency was maintained even after a temperature change from 40°C to 25°C in water.
- B: Slight turbidity was observed after a temperature change from 40°C to 25°C in water, but excellent transparency was maintained after a temperature change from 40°C to 35°C.
- C: Turbidity was remarkable after a temperature change from 40°C to 25°C in water, and turbidity was observed even after a temperature change from 40°C to 35°C.
- D: Turbidity was remarkable even after a temperature change from 40°C to 35°C in water.
- E: Irrespective of the temperature change, the material was turbid and opaque from the beginning.

[0066] Such evaluation of glistenings was carried out based on the temperature change which is believed to take place in the eye when the intraocular lens is actually implanted in the eye of a human being by an ophthalmic surgery. Namely, when an intraocular lens at room temperature, is implanted in the eye of a human being, the temperature in the eye rises to about 40°C by inflammation, and when the inflammation ceases, the temperature in the eye recovers and lowers to the body temperature, whereby the intraocular lens is considered to undergo glistenings. Accordingly, glistenings were examined during the temperature drop from such 40°C to 35°C or 25°C, which is larger than the temperature drop to a usual body temperature of from 36 to 37°C.

(c) Flexibility

[0067] The soft intraocular lens material in a dried state was folded into two at 25°C by means of tweezers, whereupon the folded state was evaluated in accordance with the following evaluation standards.

Evaluation standards

[0068]

- A: It can be readily folded without exerting any extra force.
- B: It can be readily folded by exerting a slight force.
- C: It can be folded, but a substantial extra force is required.
- D: It can hardly be folded.

(d) Shape restoration property

[0069] The soft intraocular lens material was folded back into two by means of tweezers, and held in that state for 1 minute, whereupon the material was released, and the state at that time was evaluated in accordance with the following evaluation standards.

Evaluation standards**[0070]**

- 5 A: The time required to recover to the initial shape, was less than 30 seconds.
 B: The time required to recover to the initial shape was at least 30 seconds and less than 1 minute.
 C: The time required to recover to the initial shape was at least 1 minute and less than 3 minute.
 D: The time required to recover to the initial shape was at least 3 minutes, or the material was not recovered to the
 10 initial shape.

Table 3

15	Example No.	Physical properties of soft intraocular lens materials			
		Water absorptivity (wt%)	Transparency (evaluation of glistening)	Flexibility	Shape restoration property
	1	2.3	A	A	A
	2	3.5	A	A	A
20	3	2.1	A	A	A
	4	3.3	A	A	A
	5	1.7	A	A	A
	6	1.8	A	A	A
25	7	1.8	A	A	A
	8	2.2	A	A	A
	9	2.7	A	A	A
30	10	2.5	A	B	B
	11	4.4	A	B	B
	12	1.8	B	A	A
35	13	2.8	A	A	A
	14	2.4	A	B	B
	15	3.9	A	B	B
	16	2.3	A	B	B
40	17	4.1	A	B	B
	18	1.7	B	A	A
	19	1.7	A	A	A
45	20	2.0	A	A	B
	21	2.3	A	A	A
	Comparative Example No.				
50	1	0.4	C	A	A
	2	0.3	C	A	A
	3	0.7	C	A	A
	4	0.4	C	A	A
55	5	1.1	C	A	A
	6	6.9	A	C	C

[0071] It is evident from the results shown in Table 3 that the soft intraocular lens materials obtained in Examples 1 to 21 have water absorptivities of from 1.7 to 4.4 wt%, whereby excellent transparency is maintained without glistenings, even after a temperature drop of from 5 to 15°C, and they are excellent also in the flexibility and the shape restoration properties.

5 [0072] Particularly, it is evident that in Examples 1 to 11 and 19 to 21, wherein 2-hydroxyethyl methacrylate is used as the hydrophilic monomer (B), the obtained soft intraocular lens materials are free from glistenings even after a temperature drop of 15°C.

[0073] Whereas, with the soft intraocular lens materials obtained in Comparative Examples 1 to 5, the water absorptivity of each of them is less than 1.5 wt%, and formation of glistening is remarkable.

10 [0074] Further, with the material obtained in Comparative Example 6, the water absorptivity exceeds 4.5 wt%, and it is inferior in the flexibility and the shape restoration property, although no formation of glistenings is observed.

[0075] Further, in Comparative Examples 3 and 5, glistenings were observed in spite of the fact that the hydrophilic monomer (B) was used. Accordingly, it is evident that the effect to suppress formation of glistenings, is obtainable when the material has units derived from the hydrophilic monomer (B), and the water absorptivity has a specific value of from 1.5 to 4.5 wt%, particularly at least 1.5 wt%.

[0076] Then, dumbbell-shaped test specimens were prepared from the soft intraocular lens materials obtained in Example 5 and Comparative Example 4, and tensile tests of the test specimens were carried out at a tensile speed of 100 mm/min by means of a tensile strength tester (Model 4301, manufactured by INSTRON Japan K.K.), whereby the elongation (%) at breakage was measured.

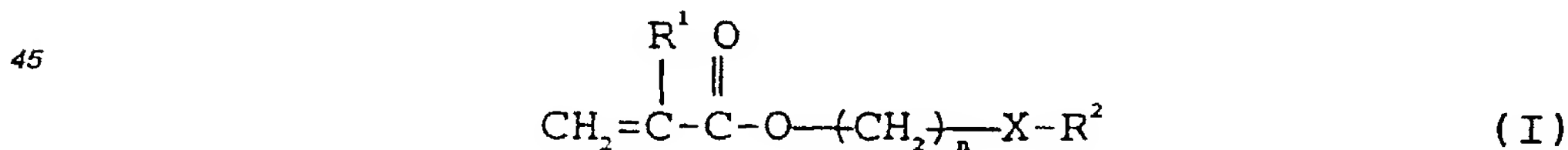
15 [0077] As a result, the elongation of the test specimen of Example 5 was 143%, and that of the test specimen of Comparative Example 4 was 94%. Thus, it is evident that the soft intraocular lens material of Example 5 is excellent in flexibility and has good mechanical strength.

[0078] As described in the foregoing, the soft intraocular lens material of the present invention is excellent in flexibility and has a high refractive index, whereby the lens can be made thin and can be folded and inserted from a small incision, and yet it is capable of presenting a soft intraocular lens which is excellent in transparency and free from glistenings.

Claims

- 30 1. A soft intraocular lens material which consists essentially of a polymer obtained by polymerizing polymerizable components containing a hydrophilic monomer, and which has a water absorptivity of from 1.5 to 4.5 wt%.
2. The soft intraocular lens material according to Claim 1, wherein the hydrophilic monomer is at least one monomer selected from a hydroxyl group-containing alkyl (meth)acrylate wherein the alkyl group has from 1 to 20 carbon atoms, a (meth)acrylamide monomer and an N-vinyl lactam.
- 35 3. The soft intraocular lens material according to Claim 2, wherein the hydroxyl group-containing alkyl (meth)acrylate wherein the alkyl group has from 1 to 20 carbon atoms, is 2-hydroxyethyl methacrylate.
4. The soft intraocular lens material according to Claim 1, wherein the polymerizable components comprise:

(A) an aromatic ring-containing (meth)acrylate of the formula (I):



- 50 wherein R¹ is a hydrogen atom or a methyl group, R² is an aromatic group wherein hydrogen atoms may be substituted by substituents, X is an oxygen atom or a direct bond, and n is an integer of from 0 to 5,
- (B) at least one hydrophilic monomer selected from a hydroxyl group-containing alkyl (meth)acrylate wherein the alkyl group has from 1 to 20 carbon atoms, a (meth)acrylamide monomer and an N-vinyl lactam,
- (C) an alkyl(meth)acrylate wherein the alkyl group has from 1 to 20 carbon atoms, other than the above
- 55 hydroxyl group-containing alkyl (meth)acrylate wherein the alkyl group has from 1 to 20 carbon atoms, and
- (D) a crosslinkable monomer.

5. The soft intraocular lens material according to Claim 4, wherein the aromatic ring-containing (meth)acrylate (A) of

the formula (I) is at least one member selected from phenoxyethyl acrylate, phenylethyl acrylate and benzyl acrylate.

- 5 6. The soft intraocular lens material according to Claim 4 or 5, wherein the hydroxyl group-containing alkyl (meth)acrylate wherein the alkyl group has from 1 to 20 carbon atoms, is 2-hydroxyethyl methacrylate.
7. The soft intraocular lens material according to Claim 4, 5 or 6, wherein the alkyl (meth)acrylate (C) wherein the alkyl group has from 1 to 20 carbon atoms, other than the hydroxyl group-containing alkyl (meth)acrylate wherein the alkyl group has from 1 to 20 carbon atoms, is ethyl acrylate and/or butyl acrylate.
- 10 8. The soft intraocular lens material according to Claim 4, 5, 6 or 7, wherein the crosslinkable monomer (D) is butane-
diol di(meth)acrylate or ethylene glycol di(meth)acrylate.
- 15 9. The soft intraocular lens material according to Claim 1 or 4, which further contains an ultraviolet absorber and/or a
yellow or orange dyestuff.

20

25

30

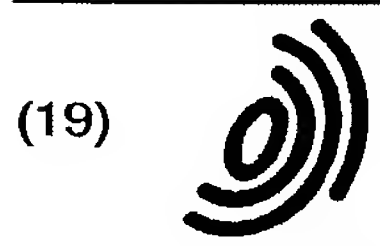
35

40

45

50

55



(19)

Europäisches Patentamt

European Patent Office

Office européen des brevets



(11)

EP 0 898 972 A3

(12)

EUROPEAN PATENT APPLICATION

(88) Date of publication A3:
27.09.2000 Bulletin 2000/39

(51) Int. Cl.⁷: **A61L 27/00**

(43) Date of publication A2:
03.03.1999 Bulletin 1999/09

(21) Application number: **98115184.8**

(22) Date of filing: **12.08.1998**

(84) Designated Contracting States:
**AT BE CH CY DE DK ES FI FR GB GR IE IT LI LU
MC NL PT SE**
Designated Extension States:
AL LT LV MK RO SI

(30) Priority: **20.08.1997 JP 22404997**

(71) Applicant: **Menicon Co., Ltd.**
Nagoya-shi Aichi-ken (JP)

(72) Inventors:
• **Ojio, Tatsuya**
Kasugai-shi, Aichi (JP)

• **Niwa, Kazuharu**
Kasugai-shi, Aichi (JP)
• **Kawaguchi, Tohru**
Kasugai-shi, Aichi (JP)

(74) Representative:
Hartz, Nikolai F., Dr. et al
Wächtershäuser & Hartz,
Patentanwälte,
Tal 29
80331 München (DE)

(54) **Soft intraocular lens material**

(57) A soft intraocular lens material which consists essentially of a polymer obtained by polymerizing polymerizable components containing a hydrophilic monomer, and which has a water absorptivity of from 1.5 to 4.5 wt%.

EP 0 898 972 A3



European Patent
Office

EUROPEAN SEARCH REPORT

Application Number
EP 98 11 5184

DOCUMENTS CONSIDERED TO BE RELEVANT			
Category	Citation of document with indication, where appropriate, of relevant passages	Relevant to claim	CLASSIFICATION OF THE APPLICATION (Int.Cl.6)
X	US 5 545 828 A (KEITA GABRIEL ET AL) 13 August 1996 (1996-08-13) * claims *	1-9	A61L27/00
X	EP 0 379 146 A (MENICON CO LTD) 25 July 1990 (1990-07-25) * page 5, line 23 - line 24 * * claims *	1-9	
X	EP 0 657 751 A (MENICON CO LTD) 14 June 1995 (1995-06-14) * page 4, line 28 - line 29 * * claims *	1-9	
			TECHNICAL FIELDS SEARCHED (Int.Cl.6)
			A61L C08F G02B G02C
The present search report has been drawn up for all claims			
Place of search THE HAGUE		Date of completion of the search 7 August 2000	Examiner Thornton, S
<p>CATEGORY OF CITED DOCUMENTS</p> <p>X : particularly relevant if taken alone Y : particularly relevant if combined with another document of the same category A : technological background O : non-written disclosure P : intermediate document</p> <p>T : theory or principle underlying the invention E : earlier patent document, but published on, or after the filing date D : document cited in the application L : document cited for other reasons & : member of the same patent family, corresponding document</p>			

EPO FORM 1503 03/82 (P04C01)

**ANNEX TO THE EUROPEAN SEARCH REPORT
ON EUROPEAN PATENT APPLICATION NO.**

EP 98 11 5184

This annex lists the patent family members relating to the patent documents cited in the above-mentioned European search report.
The members are as contained in the European Patent Office EDP file on
The European Patent Office is in no way liable for these particulars which are merely given for the purpose of information.

07-08-2000

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
US 5545828 A	13-08-1996	FR 2699541 A	24-06-1994
		US 5702825 A	30-12-1997
		AU 665473 B	04-01-1996
		AU 5254893 A	07-07-1994
		BR 9305174 A	26-07-1994
		CA 2112000 A	23-06-1994
		DE 69313997 D	23-10-1997
		DE 69313997 T	19-02-1998
		DK 605293 T	14-04-1998
		EP 0605293 A	06-07-1994
		ES 2106991 T	16-11-1997
		JP 7238120 A	12-09-1995
		US 5442022 A	15-08-1995
EP 0379146 A	25-07-1990	JP 2188717 A	24-07-1990
		JP 2716181 B	18-02-1998
		JP 2213820 A	24-08-1990
		JP 2716187 B	18-02-1998
		JP 2820438 B	05-11-1998
		JP 3043711 A	25-02-1991
		AU 615369 B	26-09-1991
		AU 4779890 A	26-07-1990
		CA 2007852 A	17-07-1990
		DE 69019382 D	22-06-1995
		DE 69019382 T	28-03-1996
EP 0657751 A	14-06-1995	JP 7157523 A	20-06-1995
		US 5519070 A	21-05-1996